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File 155:MEDLINE(R) 1966-2001/May W5
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S1 40346 HEPATITIS(W)B OR HBV OR HBVSAG
S2 154846 CONJUGAT? OR COUPL?
S3 466 S1 AND S2
S4 49 S1(3N)S2
S5 11 S1(4N)S2 NOT S4
S6 1141 PARTIC? (3N) S2
S7 16 ANTIGEN? (3N)S6
S8 43 VIRUS AND S6
S9 578 VLP OR VLPS
S10 6 GLYCOSYL? AND S9
S11 887 HPV6 OR HPV6B OR HPV(W)(6 OR 6B)
S12 15 (BACULO? OR SPODOPTERA) AND S11
S13 17 PROTEIN(W)PRESENTING
S14 1 PRESENTING(W)PLATFORM
S15 2756 RECOMBINANT? AND TARGET? AND VIRUS?
S16 56 ATTACHMENT AND S15
? t s4/7/38 46 48 49
4/7/38
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.
06905207 92059674
Phase I clinical trial of a recombinant malaria vaccine consisting of the circumsporozoite repeat region of Plasmodium falciparum coupled to hepatitis B surface antigen.
Vreden SG; Verhave JP; Oettinger T; Sauerwein RW; Meuwissen JH
Institute of Internal Medicine, University of Nijmegen, The Netherlands.
American journal of tropical medicine and hygiene (UNITED STATES) Nov 1991, 45 (5) p533-8, ISSN 0002-9637 Journal Code: 3ZQ
Languages: ENGLISH
Document type: CLINICAL TRIAL; JOURNAL ARTICLE

R16HBsAg is an experimental recombinant malaria vaccine consisting of 16 repeats of a four amino acid sequence (Asn-Ala-Asn-Pro or NANP) of the circumsporozoite (CS) protein of Plasmodium falciparum expressed as a fusion protein with the recombinant hepatitis B virus surface antigen (HBsAg) produced by yeast cells. Twenty male volunteers were experimentally vaccinated with the product, as well as with two doses of the commercial recombinant HBsAg vaccine Engerix B (Smith Kline Beecham Biologicals, Rixensart, Belgium) at intervals during a period of 18 months. No serious side effects were observed. Circulating antibodies to recombinant CS antigen (R32tet32) developed in all volunteers and persisted in most cases over ten months. Anti-HBs antibody production was poor initially, but a single dose of the commercial hepatitis B vaccine was sufficient to elevate these titers to high levels in all but two volunteers.

4/7/46
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.
04703068 85233430
A double blind study on immunotherapy with chemically modified honey bee venom: monomethoxy polyethylene glycol-coupled versus crude honey bee venom.
Muller U; Lanner A; Schmid P; Bischof M; Dreborg S; Hoigne R
International archives of allergy and applied immunology (SWITZERLAND) 1985, 77 (1-2) p201-3, ISSN 0020-5915 Journal Code: GP9
Languages: ENGLISH
Document type: CLINICAL TRIAL; CONTROLLED CLINICAL TRIAL; JOURNAL ARTICLE
24 patients with honey bee sting allergy were treated with either honey bee venom (HBV) or monomethoxy polyethylene glycol-coupled HBV (PEG-HBV) in a double blind trial. Both treatments induced a strong increase in HBV-specific IgG antibodies in most patients. Immunotherapy with PEG-HBV was much better tolerated than that with HBV. Conversely, patients on HBV did considerably better during a sting challenge with a living honey bee. Only 4 developed a large local and one a mild systemic reaction compared to 7 large local and 3 moderate to severe systemic reactions in the PEG-HBV-group. A higher maintenance dose of PEG-HBV may still be well tolerated but prove more effective at reexposure.

4/7/48
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.
04461803 83132402
Targeting of antiviral drugs by coupling with protein carriers.
Fiume L; Busi C; Mattioli A
FEBS letters (NETHERLANDS) Mar 7 1983, 153 (1) p6-10, ISSN 0014-5793 Journal Code: EUH
Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW

Side effects of antiviral drugs might be circumvented by their selective delivery into infected cells. This targeting can be obtained by conjugation of the drugs to macromolecules which are taken up specifically by the infected cells. The experiments reviewed, on this approach to antiviral chemotherapy, are mainly directed at improving the chemotherapeutic index of adenine arabinoside (ara-A) in the treatment of chronic hepatitis B by its coupling to galactosyl terminating glycoproteins. (53 Refs.)

4/7/49
DIALOG(R)File 155:MEDLINE(R)
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03823538 81192116

A method for coupling the hepatitis B surface antigen to aldehyde-fixed erythrocytes for use in passive hemagglutination.

Ikram H; Prince AM

Journal of virological methods (NETHERLANDS) Apr 1981, 2 (5) p269-75, ISSN 0166-0934 Journal Code: HQR

Languages: ENGLISH

Document type: JOURNAL ARTICLE

? t s5/7/11
5/7/11
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.
04458938 83056178

Immunogenicity of conjugates and micelles of synthetic hepatitis B surface antigen peptides.

Sanchez Y; Ionescu-Matiu II; Sparrow JT; Melnick JL; Dreesman GR

Intervirology (SWITZERLAND) 1982, 18 (4) p209-13, ISSN 0300-5526 Journal Code: GW7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A cyclic peptide containing the amino acid sequence 122 through 137 of the major hepatitis B surface antigen (HBsAg) polypeptide was synthesized. The immunogenicity of this synthetic peptide, aggregated in micelles or covalently coupled to tetanus toxoid, was assessed in mice. Antibodies against HBsAg (anti-HBs) were obtained with both preparations, administered either in saline suspension or adsorbed on aluminum gel. The peptide-tetanus toxoid conjugate was more immunogenic than the peptide micelles, producing high levels of specific anti-HBs.

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8/7/19
DIALOG(R)File 155:MEDLINE(R)
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07696756 94089670

Hepatic gene therapy: efficient gene delivery and expression in primary hepatocytes utilizing a conjugated adenovirus-DNA complex.

Cristiano RJ; Smith LC; Kay MA; Brinkley BR; Woo SL

Department of Cell Biology, Howard Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Dec 15 1993, 90 (24) p11548-52, ISSN 0027-8424 Journal Code: PV3

Contract/Grant No.: DK 44080, DK, NIDDK; HL 27341, HL, NHLBI; CA 41424, CA, NCI; +

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Receptor-mediated endocytosis is an effective method for gene delivery into target cells. We have previously shown that DNA molecules complexed with asialoglycoprotein can be efficiently endocytosed by primary hepatocytes and the internalized DNA can be released from endosomes by the use of a replication-defective adenovirus. Because the DNA and virus enter target cells independently, activity enhancement requires high concentrations of adenoviral particles. In this study, adenoviral particles were chemically conjugated to poly(L-lysine) and bound ionically to DNA molecules. Quantitative delivery to primary hepatocytes was achieved with significantly reduced viral titer when the asialoorosomucoid-poly(L-lysine) conjugate was included in the complex. The conjugated adenovirus was used to deliver a DNA vector containing canine factor IX to mouse hepatocytes, resulting in the expression of significant concentrations of canine factor IX in the culture medium. The results suggest that receptor-mediated endocytosis coupled with an efficient endosomal lysis vector should permit the application of targeted and efficient gene delivery into the liver for gene therapy of hepatic deficiencies.

8/7/22
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.
07331833 93184479

Poly(L-lysine)-conjugated oligonucleotides promote sequence-specific inhibition of acute HIV-1 infection.

Degols G; Leonetti JP; Benkirane M; Devaux C; Lebleu B

Laboratoire de Biochimie des Proteines, UA CNRS 1191, Universite de Montpellier II, Sciences et Techniques du Languedoc, France.

Antisense research and development (UNITED STATES) Winter 1992, 2 (4) p293-301, ISSN 1050-5261 Journal Code: BI7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Previously, we have reported that conjugation of antisense oligonucleotides to poly(L-lysine) (PLL) lowers their inhibitory concentration in several biological models. We have now tested these conjugates for inhibition of human immunodeficiency virus type 1 (HIV-1) replication. PLL-conjugated oligonucleotides complementary to the translation initiation site of Tat protein protect cells from the

cytopathic effect of HIV-1 in acute infection assays. The EC50 of conjugates is approximately 0.15 microM, which represents a strong reduction in concentration as compared to nonconjugated oligonucleotides (EC50 = 20 microM). In contrast with most reports in the literature, we have observed sequence specific antiviral effects with PLL conjugates. This was particularly noteworthy in antiviral experiments performed with HIV-1 isolates presenting heterogeneity in the 5' end of the tat mRNA sequence. Two mismatches at the target site were sufficient to reduce very significantly the antiviral activity of the conjugates but did not modify the effect of nonconjugated oligonucleotides. Unlike free oligonucleotides, PLL-conjugated ones do not interfere with virus penetration and/or reverse transcription as demonstrated by polymerase chain reaction (PCR) analysis of viral DNA.

8/7/24
DIALOG(R)File 155:MEDLINE(R)

06845473 92110463
Preparation of nucleoside-LDL-conjugates for the study of cell-selective internalization: stability characteristics and receptor affinity.
Schultis HW; von Baeyer H; Neitzel H; Riedel E
Institut fur Biochemie, Freie Universitat Berlin, Germany.
European journal of clinical chemistry and clinical biochemistry (GERMANY) Oct 1991, 29 (10) p665-74, ISSN 0939-4974 Journal Code: A3C
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Antiviral therapy of human immunodeficiency virus (HIV) infection is currently based on inhibition of reverse transcriptase by dideoxynucleosides, such as azidothymidine. Because of widespread toxicity it is reasonable to selectively target these drugs to infected cells. This may be accomplished utilizing drug-LDL conjugates, which are internalized via cell specific receptor pathways. With respect to HIV infection, scavenger receptors of the macrophage system seems to offer a hopeful perspective. This pathway requires chemical modification of surface polarity of the LDL. Cell experiments were conducted in HepG2 hepatocytes, which express apolipoprotein B receptors, and in P388 macrophages, which express scavenger receptors. LDL particles to be conjugated were isolated from blood donor plasma and from LDL-apheresis waste material. Non-covalent LDL conjugation with amphiphilic nucleoside derivatives produced only an unspecific nucleoside transfer to cell membranes, due to instability of the LDL conjugates. An experimental method (coincubation test) was developed to identify those conjugates that are stable in the presence of other lipophilic compartments. Covalent coupling of nucleosides to the apolipoprotein B moiety of LDL particles resulted in stable conjugates. As a consequence, the surface charge became negative, and the LDL displayed scavenger receptor affinity rather than apolipoprotein B receptor affinity. Selective targeting of nucleosides to macrophages can be accomplished by covalent coupling to LDL.

8/7/27
DIALOG(R)File 155:MEDLINE(R)

06626628 90281601
Ubiquitinated conjugates are found in preparations of several plant viruses.
Hazelwood D; Zaitlin M
Department of Plant Pathology, Cornell University, Ithaca, New York 14853.
Virology (UNITED STATES) Jul 1990, 177 (1) p352-6, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Recently D.D. Dunigan, R.G. Dietzgen, J.E. Schoelz, and M. Zaitlin (Virology 165, 310-312, 1988) demonstrated that a small proportion of the subunits of tobacco mosaic virus particles were conjugated with the small protein ubiquitin. We have now detected ubiquitinated conjugates in immunoblots of virion preparations of several other plant viruses, using anti-human ubiquitin antiserum. Based on their polyacrylamide gel migrations, plant virus-associated ubiquitin-immunoreactive proteins were considered to be possible virus structural protein-ubiquitin conjugates of the following viruses: barley stripe mosaic, brome mosaic, cowpea mosaic (two proteins), cowpea severe mosaic (two proteins), and satellite panicum mosaic. Ubiquitinated conjugates were not detected in immunoblots of preparations of cucumber mosaic virus and Cymbidium mosaic virus. The significance of ubiquitinated viral proteins remains to be determined.

8/7/32
DIALOG(R)File 155:MEDLINE(R)

04508379 84058033
Association of ganglioside-protein conjugates into cell and Sendai virus. Requirement for the HN subunit in viral fusion.
Heath TD; Martin FJ; Macher BA
Experimental cell research (UNITED STATES) Nov 1983, 149 (1) p163-75, ISSN 0014-4827 Journal Code: EPB
Contract/Grant No.: CA 32826, CA, NCI; CA 25526, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A method is described for preparing a covalent conjugate of proteins, in particular antibodies and their fragments, with gangliosides in the micellar form. The protein-ganglioside conjugate is associated with ganglioside micelles and can be separated from free protein by molecular sieve chromatography. Conjugates can irreversibly transfer from the micelle to a cell membrane of choice, and the protein portion be identified as a

new surface antigen. The successful application of this methodology has been demonstrated with three biological systems. Rabbit IgG-ganglioside conjugate has been transferred to human or sheep erythrocytes, which have been hemagglutinated with goat anti-rabbit IgG. Erythrocytes modified with ganglioside-anti-H2Kk have been shown to adhere to monolayers of L929 mouse fibroblasts which express H2Kk-antigen. Mouse monoclonal anti-glycophorin ganglioside conjugate can associate with Sendai virus and confer upon the virus the ability to agglutinate and hemolyse desialylated human erythrocytes. Using the anti-glycophorin conjugate, we demonstrated that the HN subunit, which is normally responsible for viral binding, appears also to be essential for fusion activity, because its destruction eliminates hemolysis and fusion, but not agglutination, by the conjugate-modified virus.

8/7/38
DIALOG(R)File 155:MEDLINE(R)

03598528 83058706
Association of moloney murine leukaemia virus proteins: an assay for hydrophobic protein-protein interactions.
Andersen KB
Journal of general virology (ENGLAND) Jan 1982, 58 Pt 1 p83-93, ISSN 0022-1317 Journal Code: I9B
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Protein-protein interaction of Moloney murine leukaemia virus was studied by an assay where one protein preparation was coupled covalently to Sepharose, and binding of radiolabelled proteins to the protein-Sepharose was examined. It was found that the virus proteins gp70, p30, p15E and p15 in solution could associate weakly to disrupted virus particles and to p30. However, when the disrupted virus particles and p30 were coupled to Sepharose in the presence of Triton X-100, stronger binding of the four proteins was observed. Only low or no binding of p12 and p10 was observed to these protein-Sepharoses. The results are discussed with respect to the assembly and structure of the virus particle.

8/7/40
DIALOG(R)File 155:MEDLINE(R)

03181609 77172924
Synthesis and glycosylation in vitro of glycoprotein of vesicular stomatitis virus.
Toneguzzo F; Ghosh HP
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Apr 1977, 74 (4) p1516-20, ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Coupling of ribonucleoprotein particles from L cells infected with vesicular stomatitis virus to a pre-incubated ribosomal system obtained from uninfected HeLa cells allowed synthesis of two proteins. G1 (molecular weight 63,000) and G2 (molecular weight 67,000), and all other proteins of vesicular stomatitis virus except the spike protein G (molecular weight 69,000). Analyses of the tryptic peptides showed that G1, G2, and G had identical peptide sequences. The synthesis of G2 required the presence of membranes; only G1 was synthesized in the absence of any membranes. G2 but not G1 was shown to be a glycoprotein by affinity chromatography on a concanavalin A-Sepharose column. Removal of sialic acid residues from G by neuraminidase resulted in a product having an identical mobility to G2. Digestion of G2 or G with a mixture of neuraminidase (EC 3.2.1.18), beta-galactosidase (EC 3.2.1.23), and beta-N-acetylglucosaminidase (EC 3.2.1.30), however, produced a protein of molecular weight 65,000. These data suggest that G2 is the desialated G and is formed by glycosylation of G1, which is the unglycosylated polypeptide backbone of G.

8/7/42
DIALOG(R)File 155:MEDLINE(R)

02822101 77187381
Cell surface labelling of mononuclear cells with antisera associated to turnip yellow mosaic virus of alphalpha mosaic virus particles. A freeze-etch study.
Ewijk WV; Vries ED
Histochemical journal (ENGLAND) May 1977, 9 (3) p329-40, ISSN 0018-2214 Journal Code: G9A
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Turnip yellow mosaic virus (TYMV) and alphalpha mosaic virus (AMV) were used as immuno-electron microscopical markers to detect cell surface receptors on mononuclear cells in freeze-etch replicas. TYMV particles were conjugated with vacuum-distilled glutaraldehyde to rabbit IgG anti-mouse immunoglobulins (TYMV-RAMIg conjugate) or to rabbit IgG anti-mouse theta antigen (TYMV-RAMTh conjugate). B-lymphocytes incubated with TYMV-RAMIg conjugate showed either randomly distributed particles or patches of virus particles on the etched surface of the cell membrane. Mouse thymocytes incubated with TYMV-RAMTh conjugate, however, showed only a random distribution of the virus particles. Human mononuclear cells incubated with rabbit IgG anti-AMV and AMV for the demonstration of the receptors for the Fc fragment of IgG showed the oblong shape of the AMV particles on the etched cell membrane, Fc receptors were either randomly distributed or aggregrated into patches. It is concluded that both types of virus particles are useful markers for the demonstration of membrane receptors in freeze-etch replicas of labelled cells.

8/7/43
DIALOG(R)File 155:MEDLINE(R)
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02531712 78219329
The preparation of latex particles with covalently bound polyamines, IgG and measles agglutinins and their use in visual agglutination tests.
Quash G; Roch AM; Niveleau A; Grange J; Keolouangkhot T; Huppert J
Journal of immunological methods (NETHERLANDS) 1978, 22 (1-2) p165-74, ISSN 0022-1759 Journal Code: IFE
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Carboxylated latex particles were substituted with side arms terminating in primary amine and hydrazine groups. The particles were coupled to aldehyde groups generated on glycoproteins which were treated with sodium periodate. Particles having the alipathic primary amine putrescine hapten as the sole substituent and particles linked to glycoproteins such as measles agglutinins and IgG were used to detect the presence of the corresponding antibodies or antigens in biological fluids by agglutination tests.
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$2.80 14 Type(s) in Format 7
$2.80 153 Types
$8.33 Estimated cost File155
$1.25 TYMNET
$9.58 Estimated cost this search
$9.82 Estimated total session cost 1.792 DialUnits
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File 155:MEDLINE(R) 1966-2001/May W5
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DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.
10606826 20378743
Differences in the post-translational modifications of human papillomavirus type 6b major capsid protein expressed from a baculovirus system compared with a vaccinia virus system.
Fang NX; Frazer IH; Fernando GJ
Centre for Immunology and Cancer Research, University of Queensland Department of Medicine, Princess Alexandra Hospital, Brisbane, Qld. 4102, Australia.
Biotechnology and applied biochemistry (ENGLAND) Aug 2000, 32 (Pt 1) p27-33, ISSN 0885-4513 Journal Code: AHF
Languages: ENGLISH
Document type: Journal Article
Virus-like particles (VLPs) are being currently investigated in vaccines against viral infections in humans. There are different recombinant-protein-expression systems available for obtaining the necessary VLP preparation for vaccination. However, the differences in post-translational modifications of the recombinant proteins obtained and their differences in efficacy in eliciting an anti-viral response in vaccines are not well established. In this study we have compared the post-translational modifications of human papillomavirus type-6b major capsid protein L1 (HPV 6bL1) expressed using recombinant baculovirus (rBV) in Sf9 (Spodoptera frugiperda) insect cells, with the protein expressed using recombinant vaccinia virus (rVV) in CV-1 kidney epithelial cells. Two-dimensional gel electrophoresis of biosynthetically labelled rBV-expressed HPV 6bL1 showed several post-translationally modified variants of the protein, whereas rVV-expressed HPV 6bL1 showed only a few variants. Phosphorylations were detected at threonine and serine residues for the L1 expressed from rBV compared with phosphorylation at serine residues only for the L1 expressed from rVV. HPV 6bL1 expressed using rBV incorporated [(3)H]mannose and [(3)H]galactose, whereas HPV 6bL1 expressed using rVV incorporated only [(3)H]galactose. We conclude that post-translational modification of recombinant HPV 6bL1 can differ according to the system used for its expression. Since recombinant L1 protein is a potential human-vaccine candidate, the implication of the observed differences in post-translational modifications on immunogenicity of L1 VLPs warrants investigation.
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12/7/12
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.
06636608 91073135
Expression of the full-length products of the human papillomavirus type 6b (HPV-6b) and HPV-11 L2 open reading frames by recombinant baculovirus, and antigenic comparisons with HPV-11 whole virus particles.
Rose RC; Bonnez W; Strike DG; Reichman RC
Department of Medicine, University of Rochester School of Medicine, New York 14642.

Journal of general virology (ENGLAND) Nov 1990, 71 (Pt 11) p2725-9, ISSN 0022-1317 Journal Code: I9B
Contract/Grant No.: AI-23418, AI, NIAID; AI-27658, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE

The L2 open reading frames (ORFs) of human papillomavirus (HPV) types 6b and 11 were expressed as full-length non-fusion proteins in Spodoptera frugiperda (Sf-9) cells using recombinant baculovirus. Both proteins were detected on Western blots as immunoreactive bands which migrated with apparent Mrs of 76K and 78K, respectively, and contained both cross-reactive and type-specific epitopes, as determined by polyclonal antisera directed against defined subregions of the HPV-6b and HPV-11 L2 ORFs. In addition, the minor capsid protein of HPV-11 particles co-migrates with the HPV-11 L2 ORF product and is immunoreactive with HPV-11 L2-specific antisera. These observations indicate that the anomalous electrophoretic mobilities of papillomavirus L2 ORF proteins can be explained without invoking post-transcriptional processing events and that the minor capsid protein of HPV-11 is antigenically and biophysically related to the HPV-11 L2 ORF product.

12/7/9
DIALOG(R)File 155:MEDLINE(R)

08169844 95065668

Human papillomavirus types 6 and 11 have antigenically distinct strongly immunogenic conformationally dependent neutralizing epitopes.

Christensen ND; Kirnbauer R; Schiller JT; Ghim SJ; Schlegel R; Jenson AB; Kreider JW
Department of Pathology, Milton S. Hershey Medical Center, Hershey, Pennsylvania 17033.

Virology (UNITED STATES) Nov 15 1994, 205 (1) p329-35, ISSN 0042-6822 Journal Code: XEA
Contract/Grant No.: CA56460, CA, NCI; CA47622, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Antibodies reactive to HPV types 6 and 11 were tested in ELISA and HPV-11 neutralization assays to determine whether these closely related types shared cross-reactive neutralizing epitopes. A series of HPV-11 neutralizing monoclonal antibodies (N-MAbs) that targeted conformational epitopes on infectious HPV-11 and HPV-11 L1 virus-like particles (VLPs) were tested for type-specificity of reactivity using intact HPV-6 L1 VLPs. Polyclonal antisera generated against intact HPV-6 L1 VLPs were also tested for HPV-11 neutralizing capacity using the athymic mouse xenograft system. The results demonstrated that conformationally dependent neutralizing epitopes on HPV-11 were very type-specific. Three of the four HPV-11 N-MAbs were negative for binding to HPV-6 L1 VLP, and the fourth demonstrated binding to HPV-6 L1 VLPs that was several orders of magnitude weaker than its binding to HPV-11 L1 VLP. The polyclonal anti-HPV-6 L1 VLP antiserum was only partially protective against HPV-11 infectivity even at a low dilution of 1:100. In contrast, polyclonal anti-HPV-11 L1 VLP antiserum was completely protective at dilutions greater than 1:10,000.

12/7/5
DIALOG(R)File 155:MEDLINE(R)

08633367 96187789

Epithelial cells display separate receptors for papillomavirus VLPs and for soluble L1 capsid protein.

Qi YM; Peng SW; Hengst K; Evander M; Park DS; Zhou J; Frazer IH
Papillomavirus Research Unit, University of Queensland, Princess Alexandra Hospital, Woolloongabba, Australia.

Virology (UNITED STATES) Feb 1 1996, 216 (1) p35-45, ISSN 0042-6822 Journal Code: XEA
Contract/Grant No.: R01-CA 57789-01, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

We examined the distribution of putative receptors for papillomavirus (PV) capsid proteins on various cell types, using either Hexahis HPV6b L1 fusion protein or synthetic HPV6b virus-like particles (VLPs). Specific, saturable binding of VLPs to CV-1 cells was demonstrated using 35S-labeled VLPs, with an average receptor number of 1 x 10(4)/cell and a binding affinity constant (Ka) of 4 x 10(7) M. VLP binding was quantitated by flow cytometry using a monoclonal antibody to the L1 capsid protein. Intense staining of epithelial and mesenchymal cells was observed. Some immature bone marrow-derived cells bound VLPs weakly, while the majority of B lymphoma cells demonstrated no binding. Binding to 12 of 16 VLP receptor positive cell lines was abolished by trypsin pretreatment of cells. Removal of cellular sialic acid or O-linked oligosaccharides separately did not affect VLP binding, which was enhanced about 25% when cells were pretreated with both neuraminidase and O-glycosidase. Culture of cells with sufficient tunicamycin to inhibit Concanavalin A binding did not diminish the binding of VLPs. Denatured L1 protein, either from VLPs or expressed from Escherichia coli as a Hexahis fusion protein, bound to a trypsin-resistant structure on a range of cell types and did not block the binding of VLPs to cells. Dual-fluorescence assay with a Burkitt lymphoma line BL72 demonstrated that Hexahis L1 protein and VLPs bind to separate cell surface molecules on BL72 cells. We conclude that the first binding of PV virus to cells is via a widely distributed membrane protein receptor(s) and that subsequent processing of particles may involve other non-trypsin-sensitive structure(s) also displayed on the cell membrane.

12/7/6
DIALOG(R)File 155:MEDLINE(R)

08521870 96213239
[Specific serologic studies with a novel authentic HPV antigen (virus-like particles) for HPV-6 antibodies in gynecologic patient samples]
Spezifische serologische Untersuchungen mit einem neuartigen authentischen HPV-Antigen (Virus-like Particles) auf HPV-6 Antikorper bei gynakologischen Patientenkollektiven.
Heim K; Christensen ND; Hopfl R; Wartusch B; Larcher C; Ruth N; Bergant A ; Pirschner G; Dierich MP; Kreider JW; et al
Universitatsklinik fur Frauenheilkunde, Innsbruck.
Gynakologisch-geburtshilfliche Rundschau (SWITZERLAND) 1995, 35 Suppl 1 p25-31, ISSN 1018-8843 Journal Code: BK6
Languages: GERMAN Summary Languages: ENGLISH
Document type: JOURNAL ARTICLE ; English Abstract
OBJECTIVE: A serological assay for genital HPV infection would provide important additional information to HPV DNA diagnostic methods, since it would evaluate prior exposure to the viruses, detect significant systemic immunologic response to virus infection, and could be performed in most clinical laboratories. METHODS: Serum samples from three groups of patients attending a gynecology clinic were analysed by direct ELISA for specific IgG antibodies to baculovirus-expressed HPV-6 and BPV-1-L1-VLPs. RESULTS: Positive IgG reactivity to HPV-6-L1-VLPs were 4/72 (6%) in a control group, 28/73 (38%) in a condyloma group and 17/62 (17%) in cervical intraepithelial neoplasia patients. Individual IgG ELISA values of condyloma and CIN patients for HPV-6-L1-VLPs demonstrated no correlation to results with BPV-1-L1-VLPs. CONCLUSIONS: These data show that HPV-6-L1-VLPs are effective antigens for serological studies and can detect species specific antibodies with important implications for diagnosis, epidemiology, insights to natural course of disease, prognosis and evaluation of vaccination.

12/7/7
DIALOG(R)File 155:MEDLINE(R)

08407729 96057586
Human papillomavirus (HPV) type distribution and serological response to HPV type 6 virus-like particles in patients with genital warts.
Greer CE; Wheeler CM; Ladner MB; Beutner K; Coyne MY; Liang H; Langenberg A; Yen TS; Ralston R
Chiron Corporation, Emeryville, California 94608, USA.
Journal of clinical microbiology (UNITED STATES) Aug 1995, 33 (8) p2058-63, ISSN 0095-1137 Journal Code: HSH
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Thirty-nine patients with condylomas (12 women and 27 men) attending a dermatology clinic were tested for genital human papillomavirus (HPV) DNA and for seroprevalence to HPV type 6 (HPV6) L1 virus-like particles. The L1 consensus PCR system (with primers MY09 and MY11) was used to determine the presence and types of HPV in sample specimens. All 37 (100%) patients with sufficient DNA specimens were positive for HPV DNA, and 35 (94%) had HPV6 DNA detected at the wart site. Three patients (8%) had HPV11 detected at the wart site, and one patient had both HPV6 and -11 detected at the wart site. Thirteen additional HPV types were detected among the patients; the most frequent were HPV54 (8%) and HPV58 (8%). Baculovirus-expressed HPV6 L1 virus-like particles were used in enzyme-linked immunosorbent assays to determine seroprevalence among the patients with warts. Seronegativity was defined by a control group of 21 women who were consistently PCR negative for HPV DNA. Seroprevalence was also determined for reference groups that included cytologically normal women who had detectable DNA from either HPV6 or HPV16 and women with HPV16-associated cervical intraepithelial neoplasia. Among the asymptomatic women with HPV6, only 2 of 9 (22%) were seropositive, compared with 12 of 12 (100%) female patients with warts. A similar trend in increased HPV6 seropositivity with increased grade of disease was found with the HPV16 DNA-positive women, whose seroprevalence increased from 1 in 11 (9%) in cytologically normal women to 6 in 15 (40%) among women with cervical intraepithelial neoplasia 1 or 3. However, only 4 of 25 (16%) male patients were seropositive.(ABSTRACT TRUNCATED AT 250 WORDS)

12/7/3
DIALOG(R)File 155:MEDLINE(R)

09427080 98156125
Production of recombinant virus-like particles from human papillomavirus types 6 and 11, and study of serological reactivities between HPV 6, 11, 16 and 45 by ELISA: implications for papillomavirus prevention and detection.
Touze A; Dupuy C; Mahe D; Sizaret PY; Coursaget P
Laboratoire d'Immunologie des Maladies Infectieuses, Faculte des Sciences Pharmaceutiques Philippe Maupas, Tours, France.
FEMS microbiology letters (NETHERLANDS) Mar 1 1998, 160 (1) p111-8, ISSN 0378-1097 Journal Code: FML
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The L1 major capsid proteins of human papillomaviruses types 6 and 11 were expressed in insect cells using recombinant baculoviruses. These L1 proteins were shown to self-assemble into virus-like particles resembling papillomavirus virions as previously observed for HPV 16 and 45. However, we observed variations in the yield of virus-like particles among the four genotypes investigated. This suggests that more than one strain of each genotype has to be investigated to obtain the high level of virus-like particle production necessary to develop HPV vaccines or serological tests. Cross-reactivities between HPV 6, 11, 16 and 45 were studied using polyclonal and monoclonal antibodies to virus-like particles, L1 proteins and synthetic peptides. Although antisera react strongly against homologous virus-like particles, there is evidence of some cross-reactivity. This

could be one of the explanations for the fact that antibodies to one genotype are detected in individuals infected with another genotype. This study also identified a linear epitope recognized by anti-HPV 16 virus-like particle sera.
? t s16/7/16 18 19

16/7/16
DIALOG(R)File 155:MEDLINE(R)

10093890 98077013
The 'adenobody' approach to viral targeting: specific and enhanced adenoviral gene delivery.
Watkins SJ; Mesyanzhinov VV; Kurochkina LP; Hawkins RE
Bristol University, Department of Oncology, Bristol Oncology Centre, UK.
Gene therapy (ENGLAND) Oct 1997, 4 (10) p1004-12, ISSN 0969-7128 Journal Code: CCE
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Recombinant adenoviruses have enormous potential as vectors for gene therapy. They have evolved an efficient method of infection and a wide host range but this leads to concerns about the specificity of gene delivery. In order to target an adenovirus type 5-based vector we have investigated an antibody approach. A virus neutralising scFv antibody fragment was isolated from a phage library and a C-terminal fusion protein with epidermal growth factor (EGF) constructed. This fusion protein, or 'adenobody', bound both to the fibre protein of the adenovirus and to the EGF receptor (EGFR) on human cells, and was able to direct adenoviral binding to the new receptor. Using this system the efficiency of viral infection was markedly enhanced and was targeted to the EGFR. The adenobody-directed infection correlated with the level of EGF receptor expressed on the cells and could be blocked by competition with pure EGF. Peptide inhibition experiments suggest that infection is mediated directly through attachment to the EGFR and does not require penton-integrin interactions. This work shows that the 'adenobody' approach can enhance the efficiency as well as target adenoviral infection and has numerous potential applications for gene therapy.

16/7/18
DIALOG(R)File 155:MEDLINE(R)

09996527 99291787
PEGylation of adenovirus with retention of infectivity and protection from neutralizing antibody in vitro and in vivo.
O'Riordan CR; Lachapelle A; Delgado C; Parkes V; Wadsworth SC; Smith AE; Francis GE
Genzyme Corporation, Framingham, MA 01701-9322, USA. coriordan@genzyme.com
Human gene therapy (UNITED STATES) May 20 1999, 10 (8) p1349-58, ISSN 1043-0342 Journal Code: A12
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Replication-defective recombinant adenovirus (Ad) vectors are under development for a wide variety of gene therapy indications. A potential limiting factor associated with virus gene therapy requiring repeated treatment is the development of a humoral immune response to the vector by the host. In animal models, there is a dose-dependent rise in neutralizing antibodies after primary vector administration, which can preclude effective repeat administration. The strategy we have developed to circumvent the neutralization of adenovirus vectors by antibodies is to mask their surface by covalent attachment of the polymer polyethylene glycol (PEG). Covalent attachment of PEG to the surface of the adenovirus was achieved primarily by using activated PEG tresylmonomethoxypolyethylene glycol (TMPEG), which reacts preferentially with the epsilon-amino terminal of lysine residues. We show that the components of the capsid that elicit a neutralizing immune response, i.e., hexon, fiber, and penton base, are also the main targets for PEGylation. Several protocols for PEGylation of an adenovirus vector were evaluated with respect to retention of virus infectivity and masking from antibody neutralization. We show that covalent attachment of polymer to the surface of the adenovirus can be achieved with retention of infectivity. We show further that PEG-modified adenovirus can be protected from antibody neutralization in the lungs of mice with high antibody titers to adenovirus, suggesting that PEGylation will improve the ability to administer Ad vectors on a repeated basis.

16/7/19
DIALOG(R)File 155:MEDLINE(R)

09913705 99252210
RGD inclusion in the hexon monomer provides adenovirus type 5-based vectors with a fiber knob-independent pathway for infection.
Vigne E; Mahfouz I; Dedieu JF; Brie A; Perricaudet M; Yeh P
CNRS-IGR-Rhone Poulenc Rorer UMR1582, Institut Gustave Roussy, 94805 Villejuif Cedex, France.
Journal of virology (UNITED STATES) Jun 1999, 73 (6) p5156-61, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Hypervariable region 5 (HVR5) is a hydrophilic, serotypically nonconserved loop of the hexon monomer which extrudes from the adenovirus (Ad) capsid. We have replaced the HVR5 sequence of Ad5 with that of heterologous peptides and studied their effects on virus viability and peptide accessibility. A poliovirus model epitope was first inserted in a series of nine "isogenic" viruses that differed in their flanking spacers. Whereas virus productivity was not profoundly altered by any of these modifications, immunoprecipitation experiments under nondenaturing

conditions demonstrated that epitope recognition by its cognate monoclonal antibody (C3 MAb) was strongly linker dependent and correlated perfectly with the ability of C3 MAb to inhibit transgene delivery and expression. An alphav-specific ligand (DCRGDCF) was then inserted in a suitable linker context to investigate whether hexon-modified capsids would enhance the transduction of cells displaying limiting amounts of the virus attachment receptors. Interestingly, although hexon has never been implicated in Ad entry, the modified virus significantly increased the transduction of human vascular smooth muscle cells in vitro. Competition experiments with 293 cells saturated with recombinant knob further indicated that the hexon-modified virus could use an additional, knob-independent pathway for entry. We concluded that genetic engineering of the Ad5 hexon monomer constitutes a novel and feasible approach to equip the virus with additional targeting ligands.

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S5 53 PARTIC? AND S4
S6 3900 PARTIC? AND ANTIGEN? AND S1
S7 3206 PY<1999 AND S6
S8 382269 CONJUGAT? OR COUPL? OR CROSS OR CROSSLINK?
S9 269 S7 AND S8
S10 39 VIRUS? AND S9
? t s5/7/13

5/7/13
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.
08773999 96351459
Hybrid hepatitis B virus core antigen as a vaccine carrier moiety: I. presentation of foreign epitopes.
Schodel F; Peterson D; Hughes J; Wirtz R; Milich D
INSERM U 80, Hopital Edouard Herriot, Lyon, France.
Journal of biotechnology (NETHERLANDS) Jan 26 1996, 44 (1-3) p91-6, ISSN 0168-1656 Journal Code: AL6
Contract/Grant No.: AI20720, AI, NIAID; AI33562, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Hepatitis B virus (HBV) core antigen (HBcAg) is a highly immunogenic subviral particle. Here, we review recent progress in the use of HBcAg as a carrier moiety for heterologous epitopes. To define surface exposed and immunogenic insertion sites for foreign epitopes in HBcAg, peptidic epitopes representing binding sites for virus neutralizing antibodies on the HBV surface antigens were inserted at different positions within HBcAg using genetic engineering in an Escherichia coli expression system (Schodel et al. (1992) J. Virol. 66, 106-114). While fusion to the N-terminus required a linker to become surface accessible, both fusion to the N-terminus and to the C-terminus was compatible with particle assembly and preserved the native antigenicity and immunogenicity of HBcAg. Fusion to an immunodominant internal site of HBcAg reduced the HBcAg immunogenicity and antigenicity and most drastically enhanced the immunogenicity of the inserted foreign epitope. This internal site of HBcAg was used to express circumsporozoite antigen (CS) repeat epitopes of two rodent malaria parasites and of Plasmodium falciparum (Schodel et al. (1994b) J. Exp. Med. 180, 1037-1046 and Schodel et al. (1995a) 95th ASM General Meeting, Washington DC, Abstr. E61). When purified from recombinant Salmonella typhimurium, the hybrid HBcAg-CS proteins were particulate and displayed CS antigenicity as well as reduced HBc antigenicity, as compared to native HBcAg. Immunization of several mouse strains with HBcAg-CS hybrid particles resulted in high titered serum anti-CS antibodies representing all murine IgG isotypes. Immunization of mice with HBcAg or HBcAg-CS particles formulated on alum, complete Freunds or incomplete Freunds adjuvant resulted in equivalent anti-CS and anti-HBc serum antibody titres. The possible influence of carrier-specific immunosuppression was examined and pre-existing immunity to HBcAg did not significantly alter the immunogenicity of hybrid HBcAg particles suggesting that they would be useful carrier moieties for repeated immunizations against multiple haptens or in immune subjects after HBV infection. Examination of T cell recognition of HBcAg-CS particles revealed that HBcAg-specific T cells were universally primed and CS-specific T cells were primed if the insert contained a CS-specific T cell recognition site. This indicates that the internal amino acid position in HBcAg is permissive for the inclusion of heterologous functional T helper as well as B cell epitopes. BALB/c mice immunized with HBcAg-CS1 were protected against P. berghei challenge to 90% and 100%, respectively, in two independent experiments. (14 Refs.)
? t s5/7/3 21 28 34 43

5/7/3
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.
09705367 98432167
Presentation of non-peptide antigens, in particular drugs, to specific T cells.
von Greyerz S; Zanni M; Schnyder B; Pichler WJ
Institute of Immunology and Allergology, Inselspital, Bern, Switzerland.
Clinical and experimental allergy (ENGLAND) Sep 1998, 28 Suppl 4 p7-11, ISSN 0954-7894 Journal Code: CEB
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Drugs are non-peptide antigens that can be recognized by specific T cells. It has been thought for many years that small molecular compounds

can only be stimulating for T cells after covalent binding to MHC-embedded peptides. As most drug-specific T cell clones can react to glutaraldehyde fixed antigen presenting cells (APC), recognition of drugs by specific T cells does not require prior uptake and processing of haptenated proteins by APC. In fact, activated T cell clones can recognize drugs associated with the MHC-peptide complex in a non-covalent way. Such a binding is reminiscent of superantigen stimulations of T cells. (20 Refs.)

5/7/21
DIALOG(R)File 155:MEDLINE(R)

07786366 93379485
Pharmacology and physiology of colloids.
Salmon JB; Mythen MG
Bloomsbury Department of Intensive Care, Middlesex Hospital, London, UK.
Blood reviews (SCOTLAND) Jun 1993, 7 (2) p114-20, ISSN 0268-960X Journal Code: BLR
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
The importance of an adequate circulating volume in the critically ill is well established. Plasma, albumin, synthetic colloids and crystalloids may all be used for volume expansion but the first two are expensive and crystalloids have to be given in much larger volumes than colloids to achieve the same effect. Synthetic colloids provide a cheaper, safe, effective alternative. There are three classes of synthetic colloid; dextrans, gelatins and hydroxyethyl starches; each is available in several formulations with different properties which affect their initial plasma expanding effects, retention in the circulation and side-effects. There is no ideal colloid but those with low molecular weights such as gelatins are more suitable for rapid, short term volume expansion whilst in states of capillary leak where longer term effects are required hydroxyethyl starches are more effective. Dextrans are as effective as the alternatives but produce more side-effects and the need to pre-treat with hapten-dextran renders them unwieldy in use. Albumin is as persistent as hydroxyethyl starch in the healthy circulation but is retained less well in states of capillary leak. It has no significant advantages over starches and is much more expensive. (51 Refs.)

5/7/28
DIALOG(R)File 155:MEDLINE(R)

06969454 91252774
The structural requirements of epitopes with IgE binding capacity demonstrated by three major allergens from fish, egg and tree pollen.
Elsayed S; Apold J; Holen E; Vik H; Florvaag E; Dybendal T
Laboratory of Clinical Biochemistry, University Hospital, University of Bergen, Norway.
Scandinavian journal of clinical and laboratory investigation. Supplementum (NORWAY) 1991, 204 p17-31, ISSN 0085-591X Journal Code: UCR
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Three major allergens from cod fish, egg white and tree pollen, were characterized by studies on their allergenic and antigenic structures. The major allergen of cod fish, Allergen M "parvalbumins pI 4.75", is composed of 113 amino acid residues with a molecular weight of 12,328 daltons. It comprised three domains, AB, CD and EF, consisting of 3 helices interspaced by one loop. Each of the loops of the CD and EF domains each coordinates one Ca2+. The antigenicity and allergenicity of Allergen M was deduced from studying the modified protein and some particular synthetic peptides. Three sites were encompassing IgE binding epitopes namely peptides 33-44, 65-74 and 88-96. A novel peptide (49-64), of the CD-domain, was demonstrated to be allergenically/antigenically active and cross reactive with birch pollen allergen, which incidentally was used as a negative control. This site encompassed two repetitive sequences (D-E-D-K) and (D-E-L-K), suggested to be mutually critical for the specificity of antibody binding. This hypothesis was reconfirmed by SPPS of several analogous peptides of region 39-64. Furthermore, peptide 88-103 of the EF-domain was similarly synthesized; it functioned as a monovalent hapten, blocking and not eliciting allergic reaction. Moreover, peptide 13-32 of domain AB, the non-calcium binding domain, was thoroughly tested. The results of PK inhibition showed clear activity and the peptide was found to function at the level of a divalent determinant. Ovalbumin (OA) is the most dominant of five major allergens of egg white and universally used as model protein. OA allergenic epitopes were shown to be mainly determined by the primary structure and depend on certain peptide chain length. The N-terminal decapeptide (OA 1-10) was shown to react with reaginic IgE. Direct skin test on egg allergic patients, showed no activity and the site was therefore concluded to encompasses one single Ig binding haptenic epitope. Peptide OA 323-339, was demonstrated to be valuable in studies of T-cell recognition of protein antigens. Three analogous peptides of this region were prepared and clearly shown to be immunogenic in rabbits and to bind specific IgE from patients allergic to egg. OA 323-339 was concluded to encompass an allergenic and antigenic epitope which was recognized by human and rabbit B-lymphocytes. Eight peptides in the region 11-122 were similarly synthesized. A test battery was performed to study this region using rabbit polyclonal antibodies and human specific IgE. Some of these sites were involved in binding of particular Ig paratopes. Five immunogenic peptides from the major allergens of tree pollen extracts (segment 23-38), were synthesized. The selection of those peptides was setteled using two algorithms for providing the optimal hydrophobicity.(ABSTRACT TRUNCATED AT 400 WORDS) (65 Refs.)

5/7/34

DIALOG(R)File 155:MEDLINE(R)
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06039198 86273706
Raising antibodies by coupling peptides to PPD and immunizing BCG-sensitized animals.
Lachmann PJ; Strangeways L; Vyakarnam A; Evan G
Ciba Foundation symposium (NETHERLANDS) 1986, 119 p25-57, ISSN 0300-5208 Journal Code: D7X
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW
The use of PPD (purified protein derivative of tuberculin) as a carrier has several significant advantages. It provides very powerful T cell help and it gives rise to virtually no antibody response against itself. This is particularly useful if it is intended to go on to make monoclonal antibodies, where the presence of a large amount of anti-carrier antibody is a nuisance! Furthermore, unlike most comparably powerful adjuvant systems, it can be used in man. PPD coupling has been used to raise antibodies to haptens and to raise T cell responses to tumour cells. It is here reported that small peptides coupled to PPD will give rise to good titres of anti-peptide antibody. For peptides that contain no cysteine, coupling has been achieved by attaching succinimidyl 4-(N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC) to the alpha-amino group of the peptide and N-succinimidyl 3-(2-pyridyldithio) propionate (SPDP) to the PPD and allowing an uncleavable bond to form between them. Data on immunization with the leucotactic nonapeptide of the alpha chain of the complement component C3 and with some oncogene-related peptides have been obtained. (53 Refs.)

5/7/43
DIALOG(R)File 155:MEDLINE(R)
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05222350 86218142
Polymeric microspheres as diagnostic tools for cell surface marker tracing.
Fornusek L; Vetvicka V
Critical reviews in therapeutic drug carrier systems (UNITED STATES) 1986, 2 (2) p137-74, ISSN 0743-4863 Journal Code: CRI
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW
The adequate expression of cell-surface receptors and antigens is an important requirement for the functional ability of living cells. A lot of different methods for cell surface marker tracing have been described; however, most of these techniques have disadvantages limiting their wide-scale utilization in routine laboratory and clinical practice. The most recent technique for these purposes, approaching near the ideal one, is based on the use of synthetic microspheric particles made of polymers which are formed mainly by emulsion or radiation polymerization of a variety of monomers. The resulting spherical particles bear hydroxyl, carboxyl, amino, or other functional groups capable of covalent binding of proteins, dyes, or chemotherapeutic agents. Fluorescent, radioactive or haptenic labels may be introduced already during the polymerization, too. There are three main fields of application of such specific labeled microspheres in cell biology: (1) detection of cell surface markers; (2) studies of phagocytosis mediated via cell surface markers; and (3) cell separation according to cell surface markers. In this review general principles of preparation and applications of polymeric microspheres in cell biology are summarized. (223 Refs.)
? t s9/7/20

9/7/20
DIALOG(R)File 155:MEDLINE(R)
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09520518 98214879
Biodegradable polymer microspheres as vaccine adjuvants and delivery systems.
Gupta RK; Chang AC; Siber GR
Massachusetts Public Health Biologic Laboratories, State Laboratory Institute, Boston, USA.
Developments in biological standardization (SWITZERLAND) 1998, 92 p63-78, ISSN 0301-5149 Journal Code: E7V
Contract/Grant No.: AI33575, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Though vaccination has been the most cost-effective way of controlling infectious diseases, the logistics of delivering at least two to three doses of conventional vaccines for primary immunization to achieve protection are difficult and compliance is frequently inadequate, particularly in developing countries. In recent years biodegradable polymer microspheres have received much attention for the purposes of controlled release of antigens, (i) to reduce the number of doses needed for primary immunization to as few as a single dose and (ii) to target an antigen to microfold cells on mucosal surfaces after oral administration or to antigen-presenting cells after parenteral inoculations. A variety of vaccine antigens have been encapsulated in microspheres usually composed of poly (lactic/glycolic) acid (PLGA). Based on the size of the microspheres, molecular weight of polymer and ratio of lactic to glycolic acid in the polymer, the antigen may be targeted to various cells of the immune system or it may form a depot at the site of injection, allowing the slow release of the antigen for extended periods. Additionally, another adjuvant may be incorporated inside microspheres together with the antigen, further enhancing or modulating the immune response to the desired type. The major problems in developing controlled-release vaccines include instability of vaccine antigens during micro-encapsulation, storage and subsequent hydration. We encapsulated tetanus toxoid (TT) and Haemophilus influenzae

type b capsular polysaccharide conjugated to TT (Hib-T) inside PLGA microspheres and evaluated the antibody levels in mice. A single injection of these micro-encapsulated vaccines elicited high antibody levels which persisted for several months. The antibody levels were similar or superior to those elicited by conventional formulations of AlPO4-adsorbed TT or soluble Hib-T conjugate vaccine. (84 Refs.)
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10/7/7
DIALOG(R)File 155:MEDLINE(R)
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09179401 97288737
Neutralizing antiviral B cell responses.
Bachmann MF; Zinkernagel RM
Department of Pathology, University of Zurich, Switzerland.
Annual review of immunology (UNITED STATES) 1997, 15 p235-70, ISSN 0732-0582 Journal Code: ALO
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC
Neutralizing antiviral B cell responses differ in various aspects from the many usually measured B cell responses specific for protein in adjuvants. In particular, such neutralizing antiviral B cell responses are more rapidly induced, reach higher titers, are longer lived, and are efficiently generated without adjuvants. Evidence is summarized here that the repetitiveness of many viral antigens is a key factor responsible for the efficiency of these B cell responses, amplifying B cells early and rapidly for potent IgM responses and also for efficient switching to IgG. The data reviewed indicate that B cells discriminate antigen patterns via the degree of surface Ig-cross-linking and use antigen repetitiveness as a self/nonself discriminator. (175 Refs.)

10/7/8
DIALOG(R)File 155:MEDLINE(R)
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08958786 97116577
Spatial structure and insertion capacity of immunodominant region of hepatitis B core antigen.
Borisova G; Borschukova Wanst O; Mezule G; Skrastina D; Petrovskis I; Dislers A; Pumpens P; Grens E
Biomedical Research and Study Centre, University of Latvia, Riga, Latvia.
Intervirology (SWITZERLAND) 1996, 39 (1-2) p16-22, ISSN 0300-5526 Journal Code: GW7
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Spatial and immunochemical elucidation of hepatitis B core antigen suggested unique organization of its major immunodominant region (MIR) localized within the central part of molecule around amino acid residues 74-83. This superficial loop was recognized as the most prospective target for the insertion of foreign epitopes ensuring maximal antigenicity and immunogenicity of the latter. MIR allowed a substantial capacity of insertions up to about 40 amino acid residues without loss of the capsid-forming ability of core particles. Vector capacity as well as structural behavior and immunological fate of inserted epitopes were dependent on their primary structure. Special sets of display vectors with retained but cross-sectioned MIR as well as with uni- and bidirectionally shortened MIR have been investigated. (23 Refs.)

10/7/13
DIALOG(R)File 155:MEDLINE(R)
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08502809 96155133
Adjuvants for human vaccines--current status, problems and future prospects.
Gupta RK; Siber GR
Massachusetts Public Health Biologic Laboratories, State Laboratory Institute, Boston 02130, USA.
Vaccine (ENGLAND) Oct 1995, 13 (14) p1263-76, ISSN 0264-410X Journal Code: X6O
Contract/Grant No.: AI33575, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Adjuvants help antigen to elicit an early, high and long-lasting immune response with less antigen, thus saving on vaccine production costs. In recent years, adjuvants received much attention because of the development of purified, subunit and synthetic vaccines which are poor immunogens and require adjuvants to evoke the immune response. With the use of adjuvants immune response can be selectively modulated to major histocompatibility complex (MHC) class I or MHC class II and Th1 or Th2 type, which is very important for protection against diseases caused by intracellular pathogens such as viruses, parasites and bacteria (Mycobacterium). A number of problems are encountered in the development and use of adjuvants for human vaccines. The biggest issue with the use of adjuvants for human vaccines, particularly routine childhood vaccines, is the toxicity and adverse side-effects of most of the adjuvant formulations. At present the choice of adjuvants for human vaccination reflects a compromise between a requirement for adjuvanticity and an acceptable low level of side-effects. Other problems with the development of adjuvants include restricted adjuvanticity of certain formulations to a few antigens, use of aluminum adjuvants as reference adjuvant preparations under suboptimal conditions, non-availability of reliable animal models, use of non-standard assays and biological differences between animal models and humans leading to the failure of promising formulations to show adjuvanticity in clinical trials. The most common adjuvants for human use today are still aluminum hydroxide and aluminum phosphate, although calcium phosphate and oil emulsions also

have some use in human vaccinations. During the last 15 years much progress has been made on development, isolation and chemical synthesis of alternative adjuvants such as derivatives of muramyl dipeptide, monophosphoryl lipid A, liposomes, QS21, MF-59 and immunostimulating complexes (ISCOMS). Other areas in adjuvant research which have received much attention are the controlled release of vaccine antigens using biodegradable polymer microspheres and reciprocal enhanced immunogenicity of protein-polysaccharide conjugates. Biodegradable polymer microspheres are being evaluated for targeting antigens on mucosal surfaces and for controlled release of vaccines with an aim to reduce the number of doses required for primary immunization. Reciprocal enhanced immunogenicity of protein-polysaccharide conjugates will be useful for the development of combination vaccines. (123 Refs.)

10/7/15
DIALOG(R)File 155:MEDLINE(R)

08428749 96004228
Penetration of solutes, viruses, and cells across the blood-brain barrier.
Brightman MW; Ishihara S; Chang L
Laboratory of Neurobiology, National Institutes of Health, Bethesda, MD 20892, USA.
Current topics in microbiology and immunology (GERMANY) 1995, 202 p63-78, ISSN 0070-217X Journal Code: DWQ
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
The aspects presented here of how solutes, viruses and cells are able to cross the BBB indicate that there must be an active interaction of endothelium with viruses and immune system cells before they can penetrate the brain and spinal cord. The axoplasmic pathway taken by lectin-solute conjugates is similar but not identical to that followed by viral particles during their retrograde or anterograde transit through the axoplasm. Both the conjugates and virus are transferred to other neurons transsynaptically but the receptor mediated transfer utilized by viruses is far more specific. Cranial nerves are involved in both the entry and egress of antigens into and out of the brain. Antigen, generated within the CNS, may be able to escape from the brain to lymphoid tissue by passing into the fluid around a cranial nerve, thence via the lymph into lymph nodes to initiate an immune response involving the CNS. (56 Refs.)

10/7/18
DIALOG(R)File 155:MEDLINE(R)

08239466 95129288
Development of oral vaccines to stimulate mucosal and systemic immunity: barriers and novel strategies.
Shalaby WS
Department of Microbiology and Immunology, Medical University of South Carolina, Charleston 29425.
Clinical immunology and immunopathology (UNITED STATES) Feb 1995, 74 (2) p127-34, ISSN 0090-1229 Journal Code: DEA
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC
Many questions regarding the induction of mucosal and humoral immunity through oral vaccination exist. Efficacy is dependent on the physicochemical properties of the antigen, the gastrointestinal environment, the presence of adjuvants, and the mode of delivery. Understanding how these factors interrelate will be critical to the development of new oral vaccines. A number of approaches are currently being studied to enhance the immune response. These include chemical conjugation, immunization with recombinant bacteria and viruses, and mucosal adjuvants. Vaccine delivery systems prepared from natural or synthetic polymers is a particularly promising area because many of the current methods to induce mucosal stimulation can be incorporated within these systems. Thus, the polymeric delivery system functions as a platform to facilitate uptake by M-cells and prolong antigen presentation and stimulation of the Peyer's patches. This Review examines some of the physiological and immunological barriers associated with oral vaccination and discusses novel strategies to overcome such barriers. (95 Refs.)

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Immunopotentiating reconstituted influenza virosomes (IRIVs) and other adjuvants for improved presentation of small antigens.
Gluck R
Department of Virology, Swiss Serum and Vaccine Institute, Berne.
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Synthetic peptides, purified subunits or inactivated small virus particles require immunopotentiation if they are to be effective vaccines. A large range of procedures to enhance immunogenicity has evolved over the last decades: aluminium salts, proteosomes, immunostimulating complexes (ISCOMs), liposomes, conjugation with bacterial products or derivatives, combination with surface-active agents or application of cytokines have been the most described classes of adjuvants. We describe here the design of an inactivated hepatitis A vaccine adjuvanted with immunopotentiating

reconstituted influenza virosomes (IRIVs). The formalin-inactivated hepatitis A particles are attached to reconstituted protein-lipid complexes consisting of a mixture of phospholipids and influenza virus glycoproteins. With this new vaccine design we combined different immunostimulating effects: immunopotentiation by phospholipid vesicles, recognition of the haemagglutinin (HA) epitopes by the immune system, binding capacity of HA to sialic acid-containing receptors of macrophages and immunocompetent cells and mediation of entry into the cytoplasm of macrophages by a membrane-fusion event triggered by HA. Hepatitis A seronegative human volunteers received one intramuscular injection with this new vaccine. There were only few mild local reactions and 14 days after vaccination 100% of the subjects were seropositive. Among the individuals (control group) who received an alum-adsorbed vaccine, 88% developed local reactions. The seroconversion rate was 44%. We conclude from these results that the IRIVs provide a new approach to the future design of adjuvanted vaccines. (19 Refs.)

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